REMARKS

The foregoing amendments and the following remarks are submitted in response to the communication dated November 20, 2003.

Status of the Claims

Claims 1-3, 5 and 8-17 are pending in the application. Claims 4, 6, 7 and 18-32, which are withdrawn from consideration have been canceled without prejudice. Claims 1-3, 5 and 8-13 have been canceled, without prejudice to further future prosecution. Claim 14 has been amended in order to more particularly point out and distinctly claim that which Applicants regard as the invention. Support for the amended claim can be found generally through Applicants' specification.

Claim Objections

The Examiner has objected to Claim 15 because the word "likestem" is recited and should read "like stem". Applicants have above cancelled Claim 15 making this objection moot.

Particularity and Distinctiveness of the Claims

The Examiner has rejected Claims 1-3, 5 and 8-17 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter applicant regards as the invention.

With regard to Claims 1, 8, 11, 12 and 15, the Examiner remarks that the claims as written are vague in the recitation of pluripotent "embryonic-like" stem cell. Claims 2, 3, 5 and 14 depend from Claim 1, Claims 9 and 10 depend from Claim 8, Claim 13 depends from Claim 12, and Claims 16 and 17 depend from Claim 15. Applicants respectfully disagree and submit that the term "embryonic-like stem cell" is clear to the skilled artisan, given the teachings and description set out in the Specification. The Specification, including at page 35, line25, through page 36, line 1, particularly and distinctly sets out the description and definition of embryonic-

like stem cell in stating that it extends to

> those cell(s) and/or cultures, clones, or populations of such cell(s) which are derived from non-embryonic or postnatal animal cells or tissue, are capable of self regeneration and capable of differentiation to cells of endodermal, ectodermal and mesodermal lineages.

The above definition sets the pluripotent embryonic-like stem cells of the present invention - or any shortened terminology used to refer to the cells of the present invention, including embryonic-like stem cells and stem cells (particularly wherein no additional characteristic or term precedes the word stem cell) - apart and distinct from other previously identified and described stem cells of various types, derivation and nature. For instance, the Specification, including at page 2, lines 20-31, at page 4, line 23 to page 5, line15, and at pages 35-38, describes and defines various particular and distinct types of characterized stem cells, including unipotent stem cells, bipotent stem cells, pluripotent endodermal stem cells, pluripotent mesenchymal stem cells, and pluripotent ectodermal stem cells. Each of these particular stem cells, which are distinct in and of themselves from the stem cells (pluripotent embryonic-like stem cells) of the present invention, have a particular lineage capacity and/or commitment. Remarkably, as described and demonstrated in the Specification, the embryonic-like pluripotent stem cells of the present invention are lineage-uncommitted and have the capacity to self-renew and to differentiate to cells of any of the endodermal, ectodermal, and mesodermal lineages. Applicants submit that the recitation embryonic-like pluripotent stem cell particularly points out and may be used to distinctly claim the subject matter Applicants regard as the invention.

The Examiner rejects Claim 1 and 8 as unclear in the term "derived from". The Examiner remarks that "although the origin of the cells is from non-embryonic or postnatal animal cells or tissue, are the cells altered such that they are different from the cells that they are originally derived from?". Applicants have above cancelled Claims 1 and 8, however, we respond to this rejection in as much as the preamble language of Claim 1 has been now included in amended Claim 14, previously dependent from Claim 1. Applicants remark that the term "derived from" refers to the source or origin of the cells as pointed out by the Examiner and not to a particular alteration of the cells. Applicants assert that it is clear to the skilled artisan

from a reading of the Specification that this term refers to the source or origin of the cells.

The Examiner rejects Claims 5, 11, 12 and 13 as unclear as written with regard to particular language of these Claims. Applicants have above cancelled Claims 5, 11, 12 and 13 and assert that these rejections are now moot.

In view of the foregoing amendments and remarks, Applicants submit that the Examiner's 112, second paragraph, rejections are obviated and should be withdrawn.

The §102 Rejections

The Examiner has rejected Claims 1, 2, 4, 8, 9 and 13 under 35 U.S.C.102(b) as being anticipated by Shamblott *et al.* [PNAS 95:13726-13731, 1998]. The Examiner cites Shamblott et al. as teaching the generation of human pluripotent stem cells from gonadal ridges and mesenteries containing primordial germ cells (PGCs) and teach that embryoid bodies collected from these cultures revealed a wide variety of differentiated cell types, including derivatives of all three embryonic germ layers. In particular, the Examiner cites the embryoid bodies, which demonstrated derivatives of the three embryonic germ layers, as anticipating the claimed invention. Applicants respectfully disagree. Anticipation is a question of fact. As defined by the Federal Circuit, "[t]o anticipate a claim a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject-matter." *PPG Industries, Inc. vs Guardian Industries Corp., 37 USPQ2d 1618 (Fed. Cir. 1996) (emphasis added).* Shamblott *et al* neither discloses every element of the rejected claims nor enables one skilled in the art to isolate or make the anticipating subject matter, specifically the claimed pluripotent embryonic-like stem cells. The embryonic-like stem cells of the present invention are distinct from the cells of Shamblott *et al* and further are not obvious from the cells of Shamblott *et al.* Shamblott *et al* does not teach or anticipate that cells capable of differentiating into derivatives of all three germ layers have been or could be isolated from non-embryonic, non-germ, or postnatal cells. Applicants' embryonic-like pluripotent stem cells are distinct from the primordial germ cells described in Shamblott *et al* in that they are isolated from non-embryonic or postnatal cells or tissue. In addition, embryonic stem cells (ES) and embryonic germ cells

(EG) cells have a disorganized and heterogeneous nature of development in culture, forming embryoid bodies (EB) which are aggregates of cells, and when these cells are implanted into animals or presented subcutaneously they form teratomas or tumors containing derivatives of all three germ layers (see Specification, including at page 4, lines 10-21). Applicants submit that the pluripotent embryonic-like stem cells of the present invention are distinct from the cells of Shamblott *et al.* and are not anticipated by Shamblott *et al.*.

The Examiner has rejected Claims 1-3, 5, 8-10 and 13 under 35 U.S.C. 102(b) as anticipated by Pittenger *et al.* [Science 284:143-147, 2 April 1999]. The Examiner asserts that the instantly claimed cells are indistinguishable from the cells disclosed by Pittenger *et al.* As noted by the Examiner, Pittenger *et al.* teaches human mesenchymal stem cells isolated from adult bone marrow. Applicants respectfully disagree. Anticipation is a question of fact. As defined by the Federal Circuit, "[t]o anticipate a claim a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject-matter." *PPG Industries, Inc. vs Guardian Industries Corp., 37 USPQ2d 1618 (Fed. Cir. 1996) (emphasis added).* Pittenger *et al* neither discloses every element of the rejected claims nor enables one skilled in the art to isolate or make the anticipating subject matter, specifically the claimed pluripotent embryonic-like stem cells. The mesenchymal stem cells of Pittenger *et al.* are found to differentiate into multiple mesenchymal lineages. In the abstract of Pittenger *et al.*, it is stated that "these adult stem cells could be induced to differentiate exclusively into the adipoctyic, chondrocytic, or osteocytic lineages". By their very nature and character, and as confirmed by the description of Pittenger *et al*, mesodermal stem cells can **only** differentiate into mesoderm and **cannot** form cells or tissues of ectodermal or endodermal origin. Applicants assert that the pluripotent embryonic-like stem cells of the present invention are distinct from the mesenchymal stem cells of Pittenger *et al* and are not anticipated by Pittenger *et al.*

The Examiner has rejected Claims 1-3, 5, 8, 9 and 13 under 35 U.S.C. 102(b) as anticipated by Prockop [Science 276:71-74, 1997]. The Examiner asserts that the instantly claimed cells are indistinguishable from the cells disclosed by Prockop. Prockop teaches the isolation of marrow stromal cells from mouse bone marrow which can be differentiated *in vitro* into osteoblasts, chondrocytes, adipocytes. Applicants respectfully submit that Prockop neither

discloses every element of the rejected claims nor enables one skilled in the art to isolate or make the anticipating subject matter, specifically the claimed pluripotent embryonic-like stem cells. Like the cells of Pittenger *et al.*, the mesenchymal stem cells (MSCs) of Prockop are found to differentiate into multiple mesenchymal lineages, including adipoctyic, chondrocytic, and osteocytic lineages. The pluripotent embryonic-like stem cells of Applicants, in contrast, can differentiate into mesenchymal, ectodermal and endodermal lineages. By their very nature and character, mesodermal stem cells can **only** differentiate into mesoderm and **cannot** form cells or tissues of ectodermal or endodermal origin. Applicants assert that the pluripotent embryonic-like stem cells of the present invention are distinct from the cells of Prockop and are not anticipated by Prockop.

In view of the foregoing amendments and remarks, Applicants submit that the Examiner's 102 rejections are obviated and should be withdrawn.

The §103 Rejection

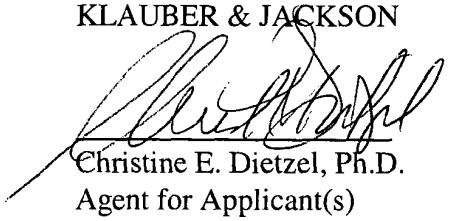
The Examiner has rejected Claims 11 and 12 under 35 U.S.C. 103(a) as being unpatentable over Pittenger *et al* [Science 284:143-147, 2 April 1999] when taken with Spector *et al.* [Cells A Laboratory Manual, Vol. 1, pp.2.12-2.13]. The Examiner asserts that, in view of the combined teachings of Pittenger and Spector, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to freeze the cells, as taught by Pittenger, using the methods taught by Spector. Applicants respectfully disagree and assert that the combination of references of Pittenger and Spector does not make obvious the invention claimed in Claims 12 and 13, particularly in view of the limited teaching in Pittenger of mesenchymal stem cells, as argued above. Applicants further point out that Claims 12 and 13 have now above been cancelled and argue that the rejection is now moot and should be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,

KLAUBER & JACKSON



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Complete Listing of Claims in Application U.S.S.N. 09/668,508

Claims 1-13 (cancelled)

14. (Amended) ~~The stem cell of Claim 1~~ A pluripotent embryonic-like stem cell, derived from non-embryonic or postnatal animal cells or tissue, capable of self-renewal and capable of differentiation to cells of endodermal, ectodermal and mesodermal lineages, genetically engineered to express a gene or protein of interest.

Claim 15 (original)

Claim 16 (original)

Claim 17 (original)

Claims 18-32 (cancelled)